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February 12, 1999

Dr. C.W. Jameson
National Toxicology Program
Report on Carcinogens
79 Alexander Drive
Room 3217
P.O. Box 12233
Research Triangle Park, NC 27709

Dear Dr. Jameson:

Philip Morris takes this opportunity to submit additional comments regarding NTP's review of Environmental Tobacco Smoke (ETS) for possible listing in the NTP *Report on Carcinogens* (RoC). The enclosed comments address procedural issues stemming from the preparation of the Background Document for ETS which was prepared for the December 2-3, 1998, meeting of the NTP Board of Scientific Counselors RoC Subcommittee. In our submission, we note several procedural inconsistencies and shortcomings that undermine the conclusions set forth in the document. NTP must rectify these procedural infirmities to ensure that ETS receives a fair and balanced review.

In light of the foregoing, Philip Morris specifically requests that NTP (i) revise the ETS Background Document to address all relevant data, including previously omitted data; (ii) refrain from relying on EPA's vacated Risk Assessment on ETS; (iii) extend the current comment period to April 1, 1999; (iv) provide for subsequent public comment on the revised ETS Background Document; and (v) convene another meeting of the Board of Scientific Counselors RoC Subcommittee with opportunity for oral public comment and questions to NTP staff who prepared and revised the Background Document.

We look forward to any additional opportunities for constructive participation in this process.

Sincerely,

Matthew N. Winokur

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NATIONAL TOXICOLOGY PROGRAM (NTP)

RE: LISTING OF ENVIRONMENTAL TOBACCO SMOKE (ETS) IN THE *REPORT ON CARCINOGENS*, NINTH EDITION

COMMENT CONCERNING PROCEDURAL ISSUES IN THE DEVELOPMENT AND USE OF NTP'S ETS BACKGROUND DOCUMENT AND THE PROPOSED LISTING OF ETS AS A KNOWN HUMAN CARCINOGEN

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I. FOREWORD

Philip Morris has demonstrated its interest in participating in a constructive manner within the general framework outlined by NTP for public participation in the agency's carcinogen listing process. In this regard, the Company has filed public comments and participated in meetings relating to the proposed listing of ETS -- to the extent NTP procedures would allow. Based upon this participation, the Company is filing these comments directed at process and procedural issues.[1]

With respect to the proposed listing of Environmental Tobacco Smoke (ETS) as a carcinogen there appear to be several recurring areas of concern:

- The public has had no opportunity, anywhere in the NTP process, to ask questions of the NTP staff members and consultants who actually drafted the Background Document on ETS;
- The public has no access to RG1 or RG2 -- all activities of these groups are shielded from public scrutiny;
- NTP's procedures, which are vague in many areas, appear to be applied inconsistently;
- NTP's decision-making regarding ETS fails to take into consideration all relevant data and even fails to explain why such data are excluded; and
- NTP relies extensively on a risk assessment that has been vacated by a federal court.

II. NTP CRITERIA FOR LISTING CARCINOGENS

A. NTP Criteria for Listing in the *Report on Carcinogens*.

In 1978, the Secretary of the Department of Health and Human Services was mandated to prepare the *Report on Carcinogens*, the Federal government's listing of agents "known" or "reasonably anticipated" to be human carcinogens. The Secretary subsequently delegated preparation of the *Report on Carcinogens* to the National Toxicology Program (NTP). In 1994, the Director of NTP initiated a review of the criteria used for listing substances, and revised criteria were issued in 1996 (61 *Fed. Reg.* 50499). The revised criteria have been used in the review of

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1. Scientific issues are discussed only in the context of these procedural implications.

nominations for listing in the Eighth *Report* (published in 1998) and the Ninth *Report* (expected to be published in 1999).

It is useful to consider the classification structure NTP has created in part to provide a background for analyzing the procedure applied to ETS and in part to offer a framework for evaluating different NTP listing decisions based upon essentially similar NTP data.

B. NTP's Classification, "Known to Be a Human Carcinogen".

The current criterion for listing in the *Report* as "known to be a human carcinogen" is stated as follows:

> There is sufficient evidence of carcinogenicity from studies in humans which indicates a causal relationship between exposure to the agent, **substance or mixture** and human cancer.[2]

This criterion provides little actual guidance to reviewers of nominations for NTP. Although the category of "studies in humans" seems to include epidemiologic studies, laboratory studies, and data on poisonings (see NTP Listing/Delisting Procedures), in many cases, only epidemiologic data are considered. However, NTP apparently provides no publicly-available, uniform guidelines as to how epidemiologic studies should be evaluated in order to determine whether they provide "sufficient evidence of carcinogenicity." It appears that "sufficient evidence of carcinogenicity" could consist of epidemiologic studies in which chance, bias or confounding are adequately excluded as alternative explanations, but how this would be done is not made clear by NTP.

C. NTP's Classification, "Reasonably Anticipated to Be a Human Carcinogen."

For NTP's second category, "reasonably anticipated to be a human carcinogen," the criteria are somewhat more complex, with a number of options.[3] However, NTP does not provide publicly available guidelines for addressing these options or for meeting this categorization.

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2. See NTP Home Page at http://ntp-server.niehs.nih.gov/ (emphasis added).

3. Although there are three NTP criteria for reaching a determination that a substance is "reasonably anticipated to be a human carcinogen," only one criterion relating to studies in humans is discussed here.

The criterion by which a substance can be classified as "reasonably anticipated" with reference to studies in humans is stated by NTP as follows:

> There is limited evidence of carcinogenicity from studies in humans, which indicates that causal interpretation is credible but that alternative explanations, such as chance, bias or confounding factors, could not adequately be excluded.

NTP's above-described criterion provides little guidance to the evaluator. NTP offers no explanation as to how it determines that chance, bias or confounding "could not adequately be excluded." It is not clear precisely how NTP would differentiate a classification of "known" from a "reasonably anticipated" classification based on the human studies criterion. This issue is significant and relevant where, as here, NTP reaches different classifications for ETS and diesel exhaust when the human study data appear to be similar.

III. INCONSISTENCIES AND SHORTCOMINGS IN THE PROCESS AND PROCEDURES CONCERNING THE NOMINATION OF ETS FOR LISTING IN NTP'S *REPORT ON CARCINOGENS* DELINEATE AN INADEQUATE BASIS FOR DECISION MAKING WITH RESPECT TO ETS

A. NTP's Background Document on ETS Does Not Satisfy Procedural Requirements for an Objective, Thorough Review.

Nominations for listing received by NTP undergo review by three committees. The first two review groups are the NIEHS/NTP Review Group (RG1), comprised of NIEHS/NTP staff scientists, and the NTP Executive Committee's Interagency Working Group (RG2), comprised of representatives of federal health research and regulatory agencies. The processes of RG1 and RG2 are not open to the public; NTP conducts these reviews behind closed doors. The third review group is the Board of Scientific Counselors Report on Carcinogens (RoC) Subcommittee, which was formed in 1996 to "broaden the scope of scientific review and broaden input to preparation of the *Report*" and to provide "external public review." (63 *Fed. Reg.* 57132) Meetings of the RoC Subcommittee are open to the public, and include time for public comments. This is the only time the public is present. At no time in the NTP process is the public allowed to question NTP on its process, procedure or science. In short, NTP has provided no opportunity for "adversarial discussion among the parties." *American Lithotripsy Soc'y* v. *Sullivan*, 785 F. Supp. 1034, 1036 (D.D.C. 1992).

NTP's Background Document on ETS was prepared by Technology Planning and Management Corporation, Durham, North Carolina. Although the Background Document should be a complete, balanced review of the relevant scientific literature on ETS, it fails in dramatic fashion to meet these objectives. For these and other reasons, the ETS Background Document does

not satisfy the procedural requirements of the Administrative Procedure Act and of NTP's Listing Procedures.

An agency must address and consider comments and input adverse to its position to avoid any appearance of prejudgment of the issue. *See, e.g., NEC Corp. v. U.S. Dept. of Commerce*, 958 F. Supp. 624, 629 (Ct. Int'l Trade 1997). In this regard, the analysis of the court in *National Small Shipments Traffic Conf., Inc. v. ICC*, 725 F.2d 1442 (D.C. Cir. 1984) appears relevant to the NTP process and procedure. That court found that, although an agency decision-making body may rely on summaries prepared by agency staff,

> [a]t some point, however, staff-prepared synopses may so distort the record that an agency decisionmaking body can no longer rely on them in meeting its obligations under the law.[4] More particularly, in informal rulemaking employing notice-and-comment procedures, dependence on severely skewed staff summaries may breach the decisionmaker's statutory duty to accord "consideration" to relevant comments submitted for the record by interested parties. See 5 U.S.C. § 553(c) (1982). Certainly, if subordinates systematically eliminated from their reports all mention of record comments adverse to the agency's final action, the consideration requirement would not be satisfied unless the decisionmakers took independent steps to familiarize themselves with withheld portions of the record. . . . This analysis suggests that petitioners do have a legal right that their comments reach Commission members in at least summary form, and that those comments be considered before final action is taken.

Id. at 1450-51. This analysis regarding staff-prepared materials is equally, if not more, pertinent to materials prepared by outside contractors -- as is the case with NTP's Background Document on ETS.

B. Procedural Shortcomings in the Background Document on ETS Disclose the Inadequacy of the Basis of NTP's Decision Making.

The major conclusion of the Draft Background Document on ETS is that ETS is "known to be a human carcinogen." Although the primary basis for this conclusion is a claimed causal relationship between ETS exposure and lung cancer risk derived from epidemiologic studies, the Background Document does not critically evaluate all studies or data. Sections from the 1986

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4. The court ruled that such distortion could conceivably result from negligence or intentional bias on the part of agency staff. *Id.* at 1451.

International Agency for Research on Cancer (IARC) Monograph on tobacco smoking,[5] the 1992 U.S. Environmental Protection Agency (EPA) Risk Assessment on ETS,[6] and the 1997 California EPA report on ETS (Cal/EPA Report)[7] are appended to the Draft Background Document, and the conclusions of these reports are discussed throughout the Background Document, suggesting heavy reliance on them by the authors. However, even these documents are not thoroughly and critically examined by NTP.

1. NTP's Reliance on IARC (1986), EPA's Report (1992) and Cal/EPA's Report (1997) Is Arbitrary, Selective and Fails to Bring Before NTP All Relevant Evidence.

- EPA's Risk Assessment. The Background Document relies heavily and uncritically on the U. S. EPA Risk Assessment on ETS, the carcinogenesis chapters and appendices of which were vacated and declared null and void by a federal district court in July 1998.[8] NTP may try to claim that it only relied on the EPA's Risk Assessment to identify studies or data for use in NTP's evaluation. However, this is precisely the problem with reliance on a vacated document. The court in vacating EPA's Report on ETS stated "EPA's study selection is disturbing." The court further stated:

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5. International Agency for Research on Cancer, *Tobacco Smoking*, Volume 38, IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans, Lyon, France, 1986.

6. U.S. Environmental Protection Agency, *Respiratory Health Effects of Passive Smoking: Lung Cancer and Other Disorders*, EPA/600/6-90/006F, January 7, 1993. On July 17, 1998, the United States District Court for the Middle District of North Carolina vacated the majority of this risk assessment. *Flue-Cured Tobacco Coop. Stabilization Corp. v. U.S. EPA*, 4 F. Supp. 2d 435 (M.D.N.C. 1998). A court order vacating agency action results in the action being annulled, set aside, rendered void and devitalized. To vacate means to "annul; to cancel or rescind; to declare, to make, or to render void; to deprive of force; to make of no authority or validity; to set aside." *Action on Smoking and Health v. Civil Aeronautics Board*, 713 F.2d 795, 797 (D.C. Cir. 1983) (internal citations omitted).

7. California Environmental Protection Agency, *Health Effects of Exposure to Environmental Tobacco Smoke*, Final Report, September 1997.

8. *See supra* note 6.

> First, there is evidence in the record supporting the accusation that EPA "cherry picked" its data. Without criteria for pooling studies into a meta-analysis, the court cannot determine whether the exclusion of studies likely to disprove EPA's *a priori* hypothesis was coincidence or intentional. Second, EPA's excluding nearly half of the available studies directly conflicts with EPA's purported purpose for analyzing the epidemiological studies and conflicts with EPA's Risk Assessment Guidelines. See ETS Risk Assessment at 4-29 ("These data should also be examined in the interest of weighing *all the available evidence*, as recommended by EPA's carcinogen risk assessment guidelines (U.S. EPA, 1986a) . . ." (emphasis added)). [9]

- IARC Monograph (1986). The Background Document implies that the 1986 IARC Monograph concluded that there was a causal association between ETS exposure and lung cancer. However, as BSC Subcommittee Reviewer Dr. Hiroshi Yamasaki of IARC correctly pointed out in his reviewer notes, the IARC Monograph did not conclude a causal relationship between ETS exposure to tobacco smoke and human lung cancer. Presumably, Dr. Yamasaki was taking into consideration the following statement found on page 314 of the 1986 IARC Monograph:

> The observations on nonsmokers that have been made so far are compatible with either an increased risk from 'passive' smoking or an absence of risk.

NTP's mischaracterization of the 1986 IARC Monograph is not only troubling but significant when one considers that the recently published report on the IARC multicenter epidemiologic study of nonsmoker lung cancer in Europe[10] is neither referenced nor discussed in the Background Document, even though it was brought to NTP's attention in public comments. This is one of the three largest ETS epidemiologic studies to be conducted to date, and reports no statistically significantly increased risk estimates for spousal,

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9. *Flue-Cured Tobacco Coop. Stabilization Corp. v. U.S. EPA*, 4 F. Supp. 2d 435, 460 (M.D.N.C. 1998).

10. Boffetta, P., et al., "Multicenter Case-Control Study of Exposure to Environmental Tobacco Smoke and Lung Cancer in Europe," *Journal of the National Cancer Institute* 90: 1440-1450, 1998.

workplace, or combined spousal and workplace exposure to ETS. Moreover, the study reports a statistically significant decrease in risk in persons exposed to ETS during childhood. If NTP is to look at human data as a basis for its classification as a known human carcinogen, under its procedures there is no logical procedural explanation for completely excluding this large, recent study.

- Cal/EPA's Report on ETS. As noted above, the Background Document relies on the Cal/EPA Report on ETS to support some of its contentions, with no discussion of the nature of the limited data upon which the Cal/EPA Report depends.[11] The Cal/EPA Report, in turn, relied on the now-vacated EPA Risk Assessment. It also predated the 1998 IARC multicenter study. Thus, Cal/EPA offers no analysis to NTP of the recent IARC data.

2. By Failing to Identify, Compile and Analyze All Pertinent Studies and Data, NTP Did Not Consider All Relevant Evidence as Required by its Guidelines.

The failure of NTP to include in its Background Document the 1998 IARC study -- one of the largest studies of ETS ever undertaken -- graphically illustrates NTP's failure to consider all relevant data, particularly when one considers that NTP routinely relies on IARC's work. NTP's failure to include this recent, relevant data becomes more problematic when the exclusion of other studies and data is considered.

- The Background Document does not critically evaluate different approaches to assessing ETS exposure, i.e., it does not list their strengths and limitations. Literature reviews, self-reports of exposure, area monitoring data and personal monitoring data are all treated equivalently. Moreover, relevant ETS exposure studies, such as those by Phillips et al. conducted in eight European cities and in Australia, are neither referenced nor discussed.[12]

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11. *See* Appendix 8 to the Submission of Philip Morris U.S.A. to the National Toxicology Program, March 20, 1998 (portion of comments to California EPA, including discussion of Cal/EPA's failure to articulate criteria for reaching conclusion of causality, and review of the limited epidemiologic studies).

12. Phillips, K., et al., "Assessment by Personal Monitoring of Respirable Suspended Particles and Environmental Tobacco Smoke Exposure for Non-Smokers in Sydney, Australia," *Indoor & Built Environment* 7: 188-203, 1998; Phillips, K., et al., "Assessment of Air Quality in Stockholm by Personal Monitoring of nonsmokers for Respirable Suspended Particles and Environmental Tobacco Smoke," *Scandinavian Journal of Work and*

(continued...)

- The Background Document states that 15 case-control studies of spousal smoking and lung cancer risk have been published since the 1986 IARC Monograph. Actually, more than 30 such studies have been published since then.[13] This suggests either that the preparers of the Background Document were not familiar with the literature in this area, or that the literature was selectively compiled, without explanation to the public of the selection criteria. The omission, whatever its origin, is not addressed, much less explained.

- Wells' meta-analysis of the workplace data[14] is cited without discussion of the validity of establishing quality criteria for study inclusion. Wells' claims about other published meta-analyses of these studies are uncritically accepted by NTP without evaluation of their merit.

- NTP states in the Background Document that "there is little or no discernible risk from exposure to ETS only during childhood." In reaching this conclusion, NTP notes that

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12. (...continued)
Environmental Health 22(Suppl.): 1-24, 1996; Phillips, K., et al., "Assessment of Air Quality in Barcelona by Personal Monitoring of Nonsmokers for Respirable Suspended Particles and Environmental Tobacco Smoke," *Environment International* 23: 173-196, 1997; Phillips, K., et al., "Assessment of Air Quality in Turin by Personal Monitoring of Nonsmokers for Respirable Suspended Particles and Environmental Tobacco Smoke," *Environment International* 23: 851-871, 1997; Phillips, K., et al., "Assessment of Environmental Tobacco Smoke and Respirable Suspended Particle Exposures for Nonsmokers in Lisbon by Personal Monitoring," *Environment International* 24: 301-324, 1998; Phillips, K., et al., "Assessment of Air Quality in Paris by Personal Monitoring of Nonsmokers for Respirable Suspended Particles and Environmental Tobacco Smoke," *Environment International* 24: 405-425, 1998; Phillips, K., et al., "Assessment of Environmental Tobacco Smoke and Respirable Suspended Particle Exposures for Nonsmokers in Prague Using Personal Monitoring," *International Archives of Occupational and Environmental Health* 71: 379-390, 1998; Phillips, K., et al., "Assessment of Personal Exposures to Environmental Tobacco Smoke in British Nonsmokers," *Environment International* 20: 693-712, 1994; Phillips, K., et al., "Measured Exposures by Personal Monitoring for Respirable Suspended Particles and Environmental Tobacco Smoke of Housewives and Office Workers Resident in Bremen, Germany," *International Archives of Occupational and Environmental Health* 71: 201-212, 1998.

13. *See, e.g.,* references cited in Appendix 8 to the Submission of Philip Morris U.S.A. to the National Toxicology Program, March 20, 1998.

14. Wells, A.J., "Lung Cancer from Passive Smoking at Work," *American Journal of Public Health* 88: 1025-1029, 1998.

"childhood cancers have been studied in both cohort and case-control studies," but goes on to conclude that "there is little consistency in their results." Because consistency of observed association is one of the Bradford-Hill criteria, NTP would have been expected to at least evaluate "no discernible risk" as manifested in the inconsistent cohort and case-control studies for adults. NTP did not.

- Relying heavily on studies by Witschi et al. in the section on animal inhalation studies, the Background Document omits relevant work by Coggins (now at Lorillard Tobacco Co.) and scientists at R.J. Reynolds,[15] and also omits relevant, recent reports by Haussmann et al. on an ongoing long-term inhalation study using room-aged sidestream smoke.[16] It appears that no attempt was made in the Background Document to synthesize, evaluate and interpret the available animal data.

- The discussion of ETS chemistry relies heavily on comparisons between, and measurements of constituents in sidestream and mainstream smoke, but fails to fully address and acknowledge the role of dilution and aging in the formation of ETS -- the complex mixture actually under consideration by NTP.

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15. *See, e.g.*, Brown, B.G., et al., "Molecular Toxicology Endpoints in Rodent Inhalation Studies," *Exp Toxic Pathol* 47: 183-191, 1995; Coggins, C.R.E., et al., "Fourteen-Day Inhalation Study in Rats, Using Aged and Diluted Sidestream Smoke from a Reference Cigarette: I. Inhalation Toxicology and Histopathology," *Fundamental and Applied Toxicology* 19: 133-140, 1992; Coggins, C.R.E., et al., "Subchronic Inhalation Study in Rats Using Aged and Diluted Sidestream Smoke from a Reference Cigarette," *Inhalation Toxicology* 5: 77-96, 1993; Lee, C.K., et al., "Fourteen-Day Inhalation Study in Rats, Using Aged and Diluted Sidestream Smoke from a Reference Cigarette: II. DNA Adducts and Alveolar Macrophage Cytogenetics," *Fundamental and Applied Toxicology* 19: 141-146, 1992; Lee, C.K., et al., "Ninety-Day Inhalation Study in Rats, Using Aged and Diluted Sidestream Smoke from a Reference Cigarette: DNA Adducts and Alveolar Macrophage Cytogenetics," *Fundamental and Applied Toxicology* 20: 393-401, 1993.

16. This work was brought to the attention of NTP in Appendix 2 of the Submission by Philip Morris U.S.A. to the National Toxicology Program, March 20, 1998. *See, e.g.*, Haussmann, H.J., et al., "12-Month Inhalation Study on Room-Aged Cigarette Sidestream Smoke in Rats," *Inhalation Toxicology* 10: 663-697, 1998; Haussmann, H.J., et al., "Comparison of Fresh and Room-Aged Cigarette Sidestream Smoke in a Subchronic Inhalation Study on Rats," *Toxicological Sciences* 41: 100-116, 1998.

- While a number of "ETS" animal studies, particularly those by Witschi et al., are summarized, the document does not contain a clear summary statement or synthesis of the "meaning" of the available experimental animal data from studies using surrogates for ETS or how these data are inconsistent with research by Hecht, upon which NTP also relies. NTP also fails to explain that reliance on data from these studies is inconsistent with NTP's prior rejection of the animal model used as inappropriate for carcinogen testing.

- The Draft Background Document does not address the relevance of tobacco smoke condensate studies to ETS. The relevance of sidestream and mainstream condensate to ETS is not discussed.

- The discussion of NNK and other TSNAs relies heavily on the work of Hecht, who is a member of the BSC Subcommittee reviewing the nomination of ETS. This is particularly troublesome when one considers that relevant work on TSNAs by Tricker and others is neither referenced nor discussed.[17]

- The discussion of studies on mutagenicity does not include a synthesis of the data or an evaluation of the quality of the studies.

The Background Document is a selective, partial review of the available data on ETS. In no way does it meet the requirements of the Administrative Procedure Act. As discussed more fully below, the agency should review the broadest possible base of information and consider all sides of the issues in conducting an objective, balanced review.

C. Procedural Shortcomings at the RoC Subcommittee Meeting Disclose a Process that Is Inconsistent and Arbitrary.

According to a recent article by two NTP staff members, "[t]he Report on Carcinogens process is now more open and is based on the best science available, thereby enhancing its use in public health policy."[18] In practice, however, the RoC Subcommittee has not conducted itself in a manner that would allow open scientific debate and discussion, nor does it seem to have

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17. *See, e.g.*, Tricker, A.R., "*N*-Nitroso Compounds and Man: Sources of Exposure, Endogenous Formation and Occurrence in Body Fluids," *European Journal of Cancer Prevention* 6: 226-268, 1997, and also other citations in Appendix 3 of the Submission by Philip Morris U.S.A. to the National Toxicology Program, March 20, 1998.

18. Lucier, G.W., and Barrett, J.C., "Public Health Policy and the National Toxicology Program," *Environmental Health Perspectives* 106: A470-A471, 1998.

worked to ensure that NTP's listing decisions are indeed based on the "best science available." If, as Lucier and Schecter assert,[19] the "overarching motivation" of NTP is "to use the best science possible in setting priorities, designing and conducting studies, and reporting results in an objective way that best meets the needs of the public and federal and state health and regulatory agencies," the RoC Subcommittee's conduct with respect to ETS has been inconsistent with this objective.

The following illustrative excerpts from the proceedings of the December 2-3, 1998, meeting of the RoC Subcommittee suggest that the Subcommittee did not follow uniformly applied procedures or a fairly administered process.[20]

- One of the most telling statements about the Subcommittee's approach to science was made by Subcommittee member Frank Mirer, who commented: "I think if we are following consistent decision rules here, which we are obviously not, but if we were to follow consistent decision rules, I think we would have -- For the epidemiology, I think it is clear that we would have to give this [diesel exhaust particulates] the same level of evidence as environmental tobacco smoke." (Transcript, December 3, 1998, p. 418) However, the Subcommittee voted to list diesel exhaust particulates as "reasonably anticipated," but ETS as "known," even after one of its own members had pointed out that to do so would be inconsistent.

- During the discussion of diesel exhaust particulates, when Subcommittee members began making comparisons with the science on ETS, that is, engaging in scientific discussion and apparently attempting to put their deliberations in context, Subcommittee Chairman Arnold Brown directed the Subcommittee: "Let's stay away from environmental tobacco smoke. We did that yesterday." (Transcript, December 3, 1998, p. 422) Comparison of the two agents might have helped the Subcommittee evaluate the inconsistencies and limitations that exist in the two data sets and assure a fair and balanced scientific treatment of each.

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19. Lucier, G.W., and Schecter, A., "Human Exposure Assessment and the National Toxicology Program," *Environmental Health Perspectives* 106: 623-627, 1998.

20. The RoC Subcommittee must comply with rules and regulations based on the Federal Advisory Committee Act (FACA), 5 U.S.C.S., Appen. § 1 et seq. FACA was established to ensure that advisory committees such as the RoC Subcommittee operate pursuant to standards and uniform procedures. In addition, pursuant to FACA, "the function of advisory committees should be advisory only" and all matters under their consideration should be determined by the agency.

- A graphic illustration of the unscientific approach condoned by the RoC Subcommittee is reflected in the statements of RoC Subcommittee member Nicholas "Kim" Hooper, California Department of Health Services. Hooper described the agents nominated for listing as "multiple murderers," "killers," and "rapists." He personified the agents as individuals one "would not invite home to babysit your daughter," given their histories. (Transcript, December 2, 1998, pp. 32-35) Hooper's characterization of the nominations, as well as his characterization of the Subcommittee as "gumshoes" collecting evidence to aid in the "sentencing" of these "not great actors," was referred to by other Subcommittee members during the course of the meeting. (See, e.g., Transcript, December 2, 1998, pp. 72 and 128) In scientific forums, such as journals or conferences, it would be considered unacceptable and inappropriate to anthropomorphize the subject being discussed.

- If NTP and the Subcommittee applied uniform procedures in pursuit of "good science," there should have been serious discussion and evaluation of relevant, recent studies, particularly if those studies were not included in the ETS Background Document. There was essentially no consideration by the Subcommittee or by NTP of the most recent major epidemiologic study on ETS exposure and lung cancer risk, the multicenter European case-control study funded by IARC. NTP staff member John Bucher, who made NTP's presentation on ETS, dismissed the IARC study as "one more study here where the odds ratios are bouncing right around 1.15, 1.2, 1.25." (Transcript, December 2, 1998, p. 179) Conversely, following a concise presentation on the IARC study by Richard Carchman of Philip Morris, there were no questions whatsoever from the Subcommittee.

- The "rules" for abstaining from voting for reasons of conflict of interest were not clear to observers. For instance, Subcommittee member Steven Belinsky abstained from voting on diesel exhaust particulates because Joe Mauderly, of a related research facility, had given a public comment. However, Stephen Hecht, whose work was relied upon heavily in the ETS Background Document and was referenced during the Subcommittee's discussions, did not abstain from the vote on ETS, even though he clearly could be said to have an "interest" in ETS, as well as to have developed a position on ETS that would not be responsive to public comments questioning aspects of the science.

- The Subcommittee's approach to unpublished data was demonstrated to be inconsistent. While NTP's Listing/Delisting Procedures clearly state that only data from publicly available, peer reviewed sources can be considered in the preparation of the sections on human studies, animal studies, genotoxicity, and mechanisms in the Background Documents, there is no stated requirement that **public comments** consist only of published data. Yet at the Subcommittee meeting, although there was discussion that unpublished data should be excluded from consideration, the treatment of unpublished data was inconsistent throughout the meeting. While some presenters on ETS were questioned about whether their work had

been published, e.g., William Butler and Ronald Marks (Transcript, December 2, 1998, p. 227), others, like James Repace, were not. In the public comment period on diesel exhaust particulates, Joe Mauderly presented what he called a "back-of-the-envelope" calculation. No one on the Subcommittee made any reference to this or suggested that it not be considered because it was unpublished. (Transcript, December 3, 1998, p. 402)

The foregoing illustrates that, at its December 1998 meeting (where the only opportunity for interaction was between stakeholders and an **advisory** committee to NTP), the BSC Subcommittee conducted itself in a manner contrary to the basic procedural requirements of the Administrative Procedure Act as well as NTP's own criteria. The listing of substances in the *Report on Carcinogens* must be based on all relevant information, including information submitted by the public; this has not occurred with respect to ETS.

D. NTP Did Not Guarantee that All Relevant Information Was Received and Considered and that the Decision Was Adequately Supported.

NTP's Listing Criteria for the *Report on Carcinogens* **mandates** that "conclusions regarding carcinogenicity in humans or experimental animals are based on scientific judgment, **with consideration given to all relevant information**" (emphasis added).

As emphasized in the foregoing sections, NTP clearly did not consider and evaluate all relevant information with respect to the agency's consideration of ETS. The Background Document should have reflected a complete literature compilation and summarization, but it did not. NTP's failure to include, evaluate and address all relevant information is a fundamental flaw in NTP's process with respect to ETS.

E. The Public's Comments Should Have Been Thoroughly Reviewed and Evaluated by NTP But Were Not.

As indicated above, it appears that NTP did not carefully review and consider the public comments, either those in writing or those submitted orally. There is no indication in the Background Document that the public comments were even reviewed by the authors of the Background Document, much less thoroughly considered and evaluated. Indeed the singular absence of any reference whatsoever to the public's comments suggests that the authors may have been instructed not to consider the public's input.

At the RoC Subcommittee meeting on December 2-3, 1998 public commenters were limited to five minutes each. After a brief break, the RoC Subcommittee voted to list ETS as a carcinogen. There was no indication that the public input tendered at the meeting was considered in any way whatsoever in the Subcommittee's decision.

F. NTP Did Not Confront and Address Adverse Facts, Data or Comments.[21]

Agencies may not "disregard those facts or issues that prove difficult or inconvenient or refuse to come to grips with certain results." *Sea Robin Pipeline Co. v. FERC*, 127 F.3d 365, 370 (5th Cir. 1997) (internal quotations omitted). *See also American Mining Congress v. U.S. EPA*, 907 F.2d 1179, 1188-89 (D.C. Cir. 1990) (setting aside EPA's decision to classify wastes as "hazardous" because EPA failed to respond adequately to commenters' challenges to EPA's testing data); *Gulf South Insulation v. U.S. Consumer Prod. Safety Comm'n*, 701 F.2d 1137, 1144-45 (5th Cir. 1983) (vacating a CPSC ban on the use of urea-formaldehyde foam because CPSC ignored commenter challenges to the data used in its risk assessment). Although required to review all sides of an issue,[22] as noted above, neither NTP nor its Background Document did this.

- NTP's Background Document was a selective compilation that apparently attempted to present only views consistent with the possibility of listing ETS as a carcinogen.

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21. To the extent that NTP failed to consider all relevant data, including adverse data, its decision could be deemed conclusory. Conclusory assertions or decisions are insufficient. *See Chemical Mfrs. Ass'n v. EPA*, 28 F.3d 1259, 1265-66 (D.C. Cir. 1994) (holding that the agency's conclusory assertions failed to rebut commenters' scientific evidence); *Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto Inc. Co.*, 463 U.S. 29, 43 (1983) (holding that an agency explanation must be rejected if it "is so implausible that it could not be ascribed to a difference in view of the product of agency expertise"); *Tanner's Council of Am., Inc. v. Train*, 540 F.2d 1188, 1193 (4th Cir. 1976) (remanding because EPA's "conclusions are the product of guesswork and not of reasoned decision-making").

22. Under the APA, NTP has a duty to ensure that its classification of ETS as a human carcinogen results from reasoned decisionmaking. This means that NTP must "fully and ably explain its course of inquiry, its analysis, and its reasoning, and show that a rational connection exists between its decision-making process and its ultimate decision." *NRDC v. U.S. EPA*, 16 F.3d 1395, 1401 (4th Cir. 1993) (internal citations omitted); *see also Appalachian Power Co. v. EPA*, 477 F.2d 495, 507 (4th Cir. 1973) (stating "the agency must in its decision explicate fully its course of inquiry, its analysis and its reasoning") (citations and quotations omitted). Only after NTP shows that it engaged in "reasoned decisionmaking" will a court defer to the Agency's scientific judgments. *Trinity Am. Corp. v. U. S. EPA*, 150 F.3d 389, 395 (4th Cir. 1998) (holding that deference is due to NTP's analysis of scientific data if NTP "fully and ably explain[s] its course of inquiry, its analysis and its reasoning") (emphasis added; internal citations and quotation marks omitted; brackets in original).

- The Background Document not only failed to contain any discussion or mention of public comments which were adverse to the concept of listing ETS as a carcinogen, but the Background Document essentially failed to address any scientific data, studies or reports adverse to a possible listing.

G. Meaningful Time and Opportunity for Comment and Questions Were Not Provided by NTP.

NTP did not provide the public with a meaningful opportunity to (i) provide comment, (ii) ask questions of NTP or (iii) respond to questions. There was no meaningful scientific "dialogue" anywhere in the process.

The only public participation in the listing process involved NTP's advisory committee (the RoC Subcommittee), not NTP. There was not one opportunity for the public to address or present comments to RG1, RG2 or directly to NTP. There were no opportunities to question NTP about (i) its Background Document; (ii) the decisions of RG1 or RG2; or (iii) any aspect of the listing process.

NTP provided no opportunity for the public to ask questions, even of the Advisory Committee, regarding the proposed listing.

H. NTP Failed to Explain Departures from Past or Present Practices in its Decision to List ETS as a Carcinogen.

Reasoned decision-making requires an agency to explain changes of policy from past decisions and apparent inconsistencies within the same decision. *Continental Air Lines, Inc. v. Civil Aeronautics Bd.*, 551 F.2d 1293, 1303 (D.C. Cir. 1977). *See also Western States Petroleum Ass'n v. EPA*, 87 F.3d 280, 284 (9th Cir. 1996) (holding that an agency "must clearly set forth the grounds for its departure from prior norms"). Diesel exhaust and ETS were investigated in parallel with regard to a proposed listing in the NTP *Report*. The processes utilized by NTP in the designation of diesel exhaust and ETS were remarkably similar, except for the result. Background Documents were prepared for both substances including discussion of human (epidemiologic) studies, animal (toxicologic) studies, and risk assessments prepared by governmental entities.

In the instance of diesel exhaust, the authors of the Background Document chose to relate the strengths and weaknesses of the human studies with emphasis on the lack of actual exposure data as a major weakness. However, the review of human studies in the ETS Background Document lacks the same sort of analysis of the studies' inherent weaknesses. The diesel exhaust Background Document contained discussion of several experimental animal studies by different

investigators while the ETS Background Document confined its review to the work of one laboratory, to the exclusion of a review of other extensive data.

The diesel exhaust Background Document relied on an IARC (1989) assessment of risk while ignoring the Cal/EPA (1998) report which identified diesel exhaust as a toxic air contaminant. The ETS Background Document contained references to the IARC (1986) assessment, the U.S. EPA (1992) assessment (Chapters 1-6 now vacated) and the Cal/EPA (1997) assessment.

These instances of unequal evaluation of diesel exhaust and ETS have resulted in the proposed classification of diesel exhaust as "reasonably anticipated to be a human carcinogen" and the proposed classification of ETS as "known to be a human carcinogen." This difference was specifically noted by committee member Franklin Mirer, when he stated that consistency would require that diesel exhaust also be classified as a "known human carcinogen" based upon the human studies.

IV. CONCLUSIONS AND RECOMMENDATIONS

Based upon the foregoing, NTP should take all of the following actions with respect to its proposed listing of ETS as a carcinogen.

1. NTP should extend to April 1, 1999, the comment period announced in 63 *Fed. Reg.* 68783-85 (December 14, 1998), to allow adequate time for public comment based upon materials, such as the transcript, which have been publicly available during only a portion of the comment period.

2. NTP should revise the ETS Background Document to address all the relevant data that have been omitted.

3. When the Background Document has been revised, NTP should provide for public comment on the revised Background Document.

4. When this process is completed, NTP should convene and provide notice of a meeting of the Board of Scientific Counselors Subcommittee. The public should be allowed an opportunity to provide written and oral testimony to the Board. In addition, NTP staff should present the revised Background Document and be available for questions from, and discussions with, the public.

5. NTP should refrain from relying on or citing EPA's vacated Risk Assessment on ETS.